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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/001,643	10/31/2001	Bradley T. Hyman	19603/3541 (CRF D-2694A)	2817

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EXAMINER	
MANTIS MERCADER, ELENI M	
ART UNIT	**PAPER NUMBER**
3737	29

DATE MAILED: 05/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/001,643	Applicant(s) HYMAN ET AL.	
	Examiner Eleni Mantis Mercader	Art Unit 3737	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-34 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-34 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 6.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

FINAL ACTION

Response to Arguments

1. Applicant's arguments with respect to claims 1-34 have been considered but are moot in view of the new ground(s) of rejection. Applicant submitted newly cited art without a statement under 37CFR 1.97 (e) which contains pertinent information to counter Applicant's arguments. The main argument is that neither Gervais nor Alfano teach simultaneous multiphoton excitation to detect neurodegenerative diseases. The Abstract by Christie et al. (Society of Neuroscience Abstracts 1998) teach simultaneous multiphoton excitation to detect neurodegenerative diseases such as Alzheimer's to enhance the ability to image amyloids deep within the living tissues by using fluorophores. Hence, this Action is made Final.

DETAILED ACTION

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gervais et al.'717 in view of Alfano et al.'386 and Christie et al. (Abstract published in Society of Neuroscience Abstracts 1998).

Gervais et al.'717 teach a method of detecting neurodegenerative diseases by detecting amyloid plaques or neurofibrillary tangles in a mammal by activating the tissue of interest,

including the brain, in-vivo and by using optical imaging under conditions effective to promote a fluorescence characteristic in order to diagnose amyloidosis related diseases such as Alzheimer's in early stages (see paragraphs 9-12, 35 and 156; describing detecting fluorescence to optically image the brain in order to diagnose diseases such as Alzheimer's).

While Gervais et al.'717 do not explicitly teach comparing the fluorescence characteristic to a standard fluorescence emitted by exciting healthy brain tissue of the mammal under the same conditions used to carryout the activating, it is well within the knowledge of skilled artisans that there has to be some type of comparison to a standard in order to determine the significance of what is being identified in the image. In other words, if there is a luminous site in the image, either comparison with a normal image or some other type of normalization will be undertaken to ensure that what is being observed is of significance. Such image processing is described by Alfano et al.'386, in col. 6, lines 17-52, wherein subtraction between images and normalization is undertaken in order to obtain a better image and thereby allow diagnosis of disease.

Photo-activation by laser and pulsed radiation are well known imaging expedients to skilled artisans.

Gervais et al.'717 in view of Alfano et al.'386 do not explicitly teach multiphoton excitation to detect neurodegenerative diseases.

In the same field of endeavor, Christie et al. (Society of Neuroscience Abstracts 1998) teach multiphoton excitation to detect neurodegenerative diseases such as Alzheimer's to enhance the ability to image amyloids deep within the living tissues by using fluorophores.

Therefore, it would have been obvious to one skilled in the art at the time that the invention was made to have modified Gervais et al.'717 in view of Alfano et al.'386 to

incorporate the teachings of Christie et al. in using multiphoton excitation as that improves the imaging of amyloids deep within the tissue.

Conclusion

3. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eleni Mantis Mercader whose telephone number is 703 308-0899. The examiner can normally be reached on Mon. - Fri., 8:00 a.m.-6:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Angela Sykes can be reached on (703) 308-5181. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Eleni Mantis Mercader
Primary Examiner
Art Unit 3737

EMM